



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,970	01/16/2004	Michael Tyo	08191-012002	6224
26161 7590 08/24/2007 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER POPA, ILEANA	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 08/24/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/758,970	Applicant(s) TYO ET AL.	
	Examiner Ileana Popa	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.
2. Claims 1, 18, and 34 have been amended. Claims 48-55 are new.
Claims 1-55 are pending and under examination.

Response to Arguments

Claim Objections

3. The objection to claim 34 for containing minor informalities is withdrawn in response to Applicant's amendment to the claim filed on 06/14/2007.

Claim Rejections - 35 USC § 103

4. Claims 1-4, 12-17, 19-25, and 32-46 remain and the new claims 48-50, 54, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah (U.S. Patent No. 6,020,004), in view of both Chen et al. (U.S. Patent No. 6,537,813) and Tice et al. (U.S. Patent 4,389,330), for the reasons of record set forth in the non-final Office action. Applicant's arguments filed 06/14/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Shah does not disclose or suggests a continuous process for microparticles preparation. Applicant argues that Shah also differs from the present invention in that it does not describe or suggest transferring an emulsion to a solvent removal device or forming an aqueous

Art Unit: 1633

suspension of nucleic acid-containing microparticles in a solvent removal device via diffusion of organic solvent into the aqueous phase of the emulsion. Applicant submits that the secondary references do not remedy the Shah's deficiencies. With respect to Chen et al., Applicant argues that they do not teach removing the organic solvent from the second emulsion to form an aqueous suspension of microparticles (claim 1, step "f"); Applicant points out that, as amended, step "f" of claim 1 recites. "forming an aqueous suspension of nucleic acid-containing microparticles in the solvent removal device via diffusion of the organic solvent into the aqueous phase of the second emulsion". With respect to Tice et al., Applicant argues that their disclosed two-step solvent removal process does not recite or suggest the formation of microparticles by removal of the solvent from the nascent microparticles via diffusion into the surrounding aqueous phase, as the amended claim 1 recites in step "f". In addition to the above, Applicant argues that one of skill in the art would not have had a reason to combine the selected steps from the distinct methods described in the cited references because Shah places a clear emphasis on the importance of using only a single step, i.e., direct lyophilization, of the final emulsion or suspension (column 6, line 66 to column 7, line3). Applicant submits that, given this emphasis, one of skill in the art would not have modified Shah's method by adding the two-step solvent removal process of Tice et al. Applicant argues that it is not clear where the process of Tice et al. could even be applied to Shah's method or what type of benefit (if any) such an addition would achieve over the direct Shah's lyophilization step. Therefore, Applicant argues, one of skill in

Art Unit: 1633

the art would not have had a motivation to combine the references and the rejection should be withdrawn.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is the combination of references that teaches a continuous process for microparticles preparation, wherein the process comprises all the steps recited in the instant claims. Although Shah does not teach a scalable continuous process, Shah teaches a process for the preparation of 0.5 μ microparticles for nucleic acid delivery, wherein the process uses the steps and components recited in claims 1, 3, 17, 25, 32-36, 41, 42, 48, and 50 (see the non-final Office action). Chen et al. teach a scaleable, concurrent flow mixing method and apparatus for the preparation of nucleic acid-containing microparticles, wherein the method and apparatus can be adapted for the mixing of more than two solutions and wherein the method and apparatus may be employed in a continuous process (see the non-final Office action). By reading Chen et al., one of skill in the art would have been motivated to modify Shah's method by using the apparatus of Chen et al. in a continuous process. One of skill in the art would have been motivated to do so because Chen et al. teach that (i) their apparatus allows for convenient, reliable, reproducible, and scaleable process that results in the production

Art Unit: 1633

of uniform quality and particle size specific for different applications and (ii) a continuous process allows for the preparation of microparticles without stopping operation of the process to load new reagents into the system. With respect to Tice et al., it is noted that they teach a two-step solvent removal method, wherein the first step involves techniques common in the art such as evaporation, heating, extraction or vacuum, followed by separation of the microcapsules from the fluid medium by filtration and removal of the remaining solvent by resuspending the microcapsules in water, wherein the water extracts the solvent from the microcapsules (see the non-final Office action), i.e., forming an aqueous suspension of nucleic acid-containing microparticles, wherein forming of the aqueous suspension takes place via diffusion of the organic solvent into the aqueous phase, as recited in claim 1, step "f". Therefore, Applicant's argument that one of skill in the art would not have been motivated to combine the cited references is not found persuasive.

With respect to the argument that one of skill in the art would lack motivation to further modify the method of Shah and Chen et al. by adding the solvent removal method of Tice et al., it is noted that, although Shah et al. teach direct lyophilization as simplifying the process, Tice et al. clearly teach their method as achieving unexpectedly higher active agent loading and microparticles quality as compared to single-step methods. For these reasons, one of skill in the art would have been motivated to sacrifice simplicity for quality, in order to achieve microparticles with superior characteristics. With respect to the limitations recited in claims 54 and 55, Chen et al. teach that both the size and uniformity is regulated by controlling the mixing ratio, flow

Art Unit: 1633

rate, and mixing rate (column 6 bridging column 7). Absent evidence of unexpected results, it would have been obvious to the ordinary skilled artisan to vary the parameters in a given method with the purpose of optimizing the results. Again, absent evidence to the contrary, it is generally not inventive to discover the optimal working conditions of a prior art method, such conditions can be identified by routine experimentation.

The limitation of the first aqueous solution comprising EDTA (claim 49), is not innovative over the prior art. It is noted that Shah teaches Tris-HCl; however, absent evidence of unexpected results, one of skill in the art would have known to use other forms of Tris, such as Tris-EDTA.

For all the reasons above, the rejection is maintained.

5. Claims 1-6, 12-17, 19-25, and 32-46 remain and the new claims 48-50, 54, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah taken with Chen et al. and Tice et al., in further view of Parikh et al. (U.S. Patent No. 5,660,858) for the reasons of record set forth in the non-final Office action. Applicant's arguments filed 06/14/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the combination of Shah, Chen et al. and Tice et al. does not render obvious the method of independent claim 1 and that Parikh et al. do not remedy this deficiency.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons stated above.

6. Claims 1-4, 7-47 remain and the new claims 48-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shah taken with Chen et al. and Tice et al., in further view of both Hartounian et al. (PGPUB 2002/0039596) and Hedley et al. (U.S. Patent 5,783,567) for the reasons of record set forth in the non-final Office action. Applicant's arguments filed 06/14/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the combination of Shah, Chen et al. and Tice et al. does not render obvious the method of independent claim 1 and that Hartounian et al. Hedley et al. do not remedy this deficiency.

Applicant's arguments are acknowledged, however, the rejection is maintained for the reasons stated above.

With respect to the limitations recited in the new claims 51-53, see the non-final Office action.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1633

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

/Joseph Woitach/
Joseph Woitach
SPE 1633